Cost-utility analysis of Canadian tailored prophylaxis, primary prophylaxis and on-demand therapy in young children with severe haemophilia A

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Record Status
This is a critical abstract of an economic evaluation that meets the criteria for inclusion on NHS EED. Each abstract contains a brief summary of the methods, the results and conclusions followed by a detailed critical assessment on the reliability of the study and the conclusions drawn.

CRD summary
The study investigated the cost-effectiveness of three strategies for the management of severe haemophilia A in young male children. The strategies were on-demand therapy, standard prophylaxis, and escalating-dose prophylaxis. Prophylaxis improved clinical outcomes and quality of life in comparison with on-demand treatment, but with substantial costs from the perspective of society. Despite some methodological weaknesses related to the sources of data, the authors’ conclusions appear to be valid.

Type of economic evaluation
Cost-effectiveness analysis, cost-utility analysis

Study objective
The objective was to compare the cost-effectiveness of three strategies for the management of severe haemophilia A in young male children. The strategies were on-demand therapy (Demand), standard prophylaxis (SP), and escalating-dose prophylaxis (EscDose). The authors hypothesised that EscDose would be less expensive and associated with fewer complications than SP, and that both strategies would be more effective but more costly than Demand.

Interventions
The Demand strategy consisted of treatment with replacement of coagulation factor VIII (FVIII) at the time of a new onset haemorrhage (40 FVIII units per kg, u/kg, upon presentation of bleeding and 20 FVIII u/kg on days one and three post-bleed).

The SP strategy consisted of FVIII replacement every other day (25 FVIII u/kg).

The EscDose strategy began with prophylaxis with 50 FVIII u/kg once a week, which was escalated to 30 FVIII u/kg twice a week if children met the escalation criteria, then the dose was further escalated to 25 FVIII u/kg on alternate days if the escalation criteria were met again.

Location/setting
Canada/community and hospital.

Methods
Analytical approach:
This economic evaluation was based on a Markov model that depicted the natural history of disease and compared the costs and benefits with the three alternative strategies. The time horizon of the analysis was five years and the authors stated that a societal perspective was adopted.

Effectiveness data:
The clinical data were derived from a selection of known, relevant studies. For example, the data on the natural history of disease (risk of bleeding without prophylaxis) came from the retrospective review of six-year charts of 24 children admitted to a Canadian hospital. This source of data was supplemented with other published studies, the details of which were not given. Prophylaxis efficacy was obtained from three non-randomised comparative studies. The primary clinical measure was the relative risk reduction of a bleeding event with the three prophylactic strategies.
Monetary benefit and utility valuations:
The utility valuations were derived from a published source which used the standard gamble approach in a general societal sample of 30 individuals.

Measure of benefit:
Quality-adjusted life-years (QALYs), joint haemorrhages avoided, and target joints avoided were used as the summary benefit measures. The benefits accumulated beyond the first year were discounted at an annual rate of 3%.

Cost data:
The analysis included the costs of FVIII, professional visits and tests, central venous placement and complications, hospitalisations, home programmes, and parents’ days off work. The unit costs were derived from the Canadian Blood Services and published studies. The data on resource use were derived from a survey of 17 Canadian clinics supplemented with published data. A 3% annual discount rate was applied to costs accrued after the first year of the model. The costs were in Canadian dollars (CAD) and the price year was 2003.

Analysis of uncertainty:
A deterministic one-way sensitivity analysis was undertaken by varying each input of the model using plausible ranges of values.

Results
Over five years, per child, the expected total costs were CAD 277,209 with Demand, CAD 443,185 with EscDose, and CAD 569,835 with SP; joint haemorrhages were 69.13 with Demand, 17.26 with EscDose, and 4.08 with SP; and QALYs were 4.17 with Demand, 4.47 with EscDose, and 4.48 with SP.

The the incremental cost per QALY gained was CAD 542,938 with EscDose versus Demand and above CAD 1,000,000 with SP versus EscDose. The incremental cost per joint haemorrhage avoided was CAD 3,192 with EscDose versus Demand and CAD 9,046 with SP versus EscDose. The incremental cost per target joint avoided was CAD 244,082 with EscDose versus Demand and CAD 361,857 with SP versus EscDose.

The sensitivity analysis showed that the most influential model inputs were the cost of FVIII, the utility of target-joint bleeding, and the disutility associated with a target joint or frequent bleeding requiring dose escalation. However, high changes in these parameters were needed to make relevant changes in the cost-effectiveness ratios.

Authors’ conclusions
The authors concluded that, in general, prophylaxis improved clinical outcomes and quality of life in comparison with on-demand treatment but with substantial costs from the perspective of society. The authors noted that further research should investigate the long-term costs and benefits of prophylactic strategies.

CRD commentary
Interventions:
The authors justified their selection of the comparators, which ranged from minimum practice (Demand), which also reflects the usual pattern of care, to the emerging gold standard (SP).

Effectiveness/benefits:
The authors gave some details of the sources used to derive the clinical data for the model. Most of the evidence came from studies with a design which was usually associated with drawbacks such as being retrospective or non-randomised. Furthermore, the authors did not discuss the issue of homogeneity among the patient populations included in these studies. The derivation of utility valuations was clearly described and the approach used to calculate QALYs was reported. The use of disease-specific and more comparable benefit measures was appropriate.

Costs:
The analysis of costs was consistent with the perspective adopted in the study. The authors described the approach used to derive cost and resource use data and their calculation. However, the costs were presented as macro-categories, often related to specific health conditions. The price year and the use of discounting were reported. The use of alternative
costs was investigated in the sensitivity analysis.

**Analysis and results:**
The synthesis of costs and benefits was appropriately performed and clearly presented. The issue of uncertainty was partially addressed in the sensitivity analysis, which was based on a deterministic approach. The results of the sensitivity analysis were selectively presented. The authors provided a clear representation of the decision model and the natural history of disease. Some limitations of the analysis were discussed.

**Concluding remarks:**
Overall, the study appears to have been based on a valid methodology although with some limitations associated with some sources of clinical data. In general, the authors’ conclusions appear to be valid.

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**Bibliographic details**

**Other publications of related interest**


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